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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/892,071	06/26/2001	Michael D. Pierschbacher	P.U.A. 4798	4768

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EXAMINER
CHISM, BILLY D

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/892,071	PIERSCHBACHER ET AL.	
	Examiner	Art Unit	
	B. Dell Chism	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-54* is/are rejected.

7)☒ Claim(s) *45* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This Office Action is in response to Paper No. 7 filed on 01 December 2002. Claims 45-54 are pending and are under consideration by the Examiner.

Objections/Rejections

New/Maintained/Withdrawn

1. (New) Claim 45 is objected to for lacking a period at the end of claim.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. (Withdrawn) Applicants have amended claims regarding the term "cell" in reference to in vivo and in vitro, thus, the rejection is withdrawn in light of amended claims.

4. (New) Claim 45 is rejected for the indefinite recitation of the phrase "other receptors" wherein it is not understood to which other receptors are Applicants referring.

5. (New) Claim 46 is rejected for depending from rejected claim 45.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. (New) Claims 46, 48, 50, 52 and 54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for in vitro methods of using a stabilized

stereochemical conformation of a cyclic RGD containing peptide, does not reasonably provide enablement for in vivo methods of use for stabilized stereochemical conformation of a cyclic RGD containing peptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to undue experimentation. The factors include:

1) the nature of the invention;
2) the breadth of the claims;
3) the predictability or unpredictability of the art
4) the amount of direction or guidance presented;
5) the presence or absence of working examples;
6) the quantity of experimentation necessary;
7) the state of the prior art; and,
8) the relative skill of those skilled in the art;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation.

1) the nature of the invention and the breadth of the claims;

The nature of the claims is for in vivo use of a stabilized stereochemical conformation of a cyclic RGD containing peptide wherein the methods of use of such a compound are for industrial uses of coating medical devices, including prostheses or implants (vascular implants).

2) the predictability or unpredictability of the art and the state of the prior art;

There is no prior art that teaches the predictability of the claimed method of in vivo use of the stabilized stereochemical conformation of a cyclic RGD containing peptide, thus, rendering in vivo methods of use unpredictable.

3) the amount of direction or guidance presented and the presence or absence of working examples;

The application does not teach how to assess and/or modify each of the variables necessary for in vivo uses. The application does not teach how to extrapolate the teachings from the specific examples of in vitro methods in the specification to all other possibilities such as in vivo uses. The specification does not provide explanation of how to avoid pitfalls in the process making and/or use of the compound.

4) *the quantity of experimentation necessary and the relative skill of those skilled in the art;*

5) It is apparent by the lack of prior art regarding the methods of in vivo use for stabilized stereochemical conformation of a cyclic RGD containing peptide that the quantity of experimentation necessary to reduce the compound to practice for in vivo uses would be undue to those skilled in the art.

In consideration of each of factors, it is apparent that there is undue experimentation because of the unpredictability of the outcome that is not addressed by the present application disclosure, examples, teaching, and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. (Maintained) Claims 45, 47, 49 and 51 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hayman *et al.* 1985 (J. Cell Biol. 100: 1948-1954). Applicants' arguments have been fully considered but they are not persuasive. Applicants argue that Hayman *et al.* does not teach all of the elements of the claimed invention because Hayman does not teach a

conformationally restricted RGD sequence. However, Applicants' specification discloses a conformationally restricted RGD sequence as provided by cyclization, by inclusion into a constraining conformational structure, or by providing an additional chemical structure (see the specification at page 3, lines 9-14). The peptide taught by Hayman *et al.* comprises additional amino acids, which are additional chemical structures. Thus, absent some evidence to the contrary, the peptide taught by Hayman *et al.* has additional chemical structures in the form of additional amino acids, thus, meets the limitations of the claimed peptides.

10. (Withdrawn) The 102(b) rejection of claim 53 is withdrawn as being anticipated by Hayman *et al.* wherein Hayman *et al.* doesn't teach enhanced affinity for the binding site by the conformationally restricted compound.

Double Patenting

11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. (New) Claims 45-54 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 45-52 and 61-68 of U.S. Patent No. 5,981,468. Claims 45-52 teach a method of inhibiting attachment of cells to a substrate comprising contacting cells with a stabilized stereochemical conformation of a cyclic RGD

containing peptide and where the RGD compound binds to the RGD binding site of a receptor of the RGD family of receptors. Although, claims 45-52 teach "substrate", it is obvious that vitronectin is a substrate. Claims 45-54 teach the inhibition of cell attachment to vitronectin which is within the scope of the patented claims 45-52.

Furthermore, claims 61-68 teach a method of inhibiting binding of a ligand to a receptor which binds an RGD sequence by contacting a stabilized stereochemical conformation of a cyclic RGD containing peptide with said receptor, thus, inhibiting the binding of ligand to the said receptor. It is obvious that vitronectin is a ligand that binds the RGD receptor binding receptor cite, thus, claims 45-54 are obvious over claims 61-68 wherein claims 45-54 teach inhibition of cell to vitronectin binding via blocking of RGD receptor cite by using the stabilized stereochemical conformation of a cyclic RGD containing peptide.

Conclusions

Due to the new grounds of rejection herein, this action is made NON-FINAL. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to B. Dell Chism whose telephone number is 703-306-5815. The examiner can normally be reached on 7:30 AM - 4:30 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 703-306-3220. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

***

B. Dell Chism
10 March 2003

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
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